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Communication

1,*n*-Bisborylalkanes via Radical Boron Migration

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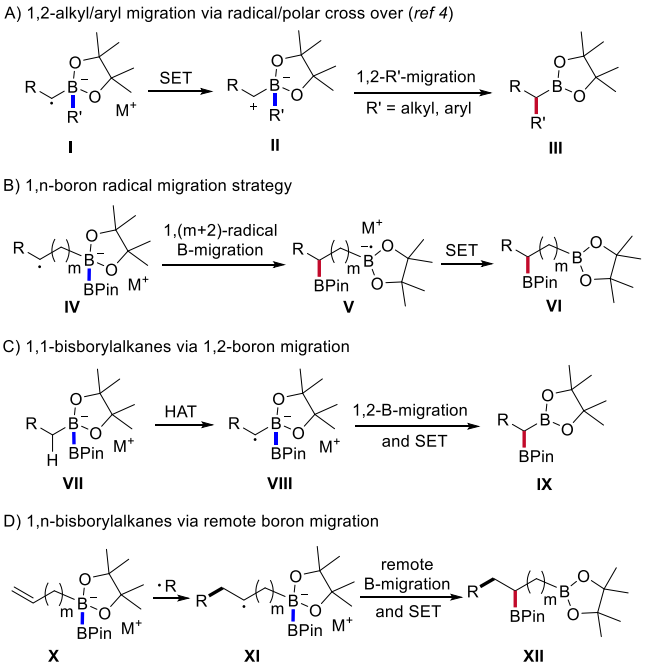
ABSTRACT: A systematic study of radical boron migration in diboronate complexes to form synthetically valuable 1,*n*-bisborylalkanes is reported. The boronate complexes are readily generated by reaction of commercial bis(pinacolato)diboron with alkyl Grignard compounds. C-radical generation at a defined position with respect to the diboron moiety is achieved either via intermolecular H-abstraction with a CF_3-radical or via alkene perfluoroalkyl radical addition. It is shown that radical 1,2- and 1,4-boron migrations to provide geminal and 1,3-bisborylalkanes are efficient transformations. The 1,5-boron migration in the homologous series leading to 1,4-bisborylalkanes is also occurring, albeit with lower efficiency. Experimental results are supported by DFT calculations which also reveal the corresponding 1,3-boron migration in such diboronate complexes to be feasible.

Bisborylalkanes are functionalized and versatile building blocks in organic synthesis. Such B-compounds can act as coupling partners in transition-metal-catalyzed cross-coupling reactions or as radical precursors, and both boryl moieties can, in principle, be selectively converted to different functionalities.[1] Boronate complexes are reactive intermediates that are readily generated by the reaction of organoboronic esters with organometallic reagents. These B-ate complexes are reducing species that also undergo facile hydrolysis.[2] Recently, radical chemistry on boronate complexes has emerged.[3] It was found that C-radicals of type **I** derived from boronate complexes are readily oxidized by single electron transfer (SET) to give zwitterions of type **II** in a radical/polar crossover step (Scheme 1A). Intermediates **II** in turn undergo a Matteson-type 1,2-alkyl/aryl shift to afford α-functionalized boronic esters **III**.[4] Although such transformations on boronate complexes generated from alkyl and aryl boronic esters are meanwhile well investigated, the corresponding radical reactions on diboronate complexes derived from diborons (see **IV**) are underdeveloped. Along these lines, Shi recently reported the construction of 1,1-bisborylalkanes enabled by radical addition/1,2-boron migration. As mechanism of the boron migration, it was proposed that diboronate complexes **IV** (m = 0) are SET-oxidized to intermediates of type **II** (R′ = BPin), which rearrange to geminal bisborylalkanes via an ionic process.[5] Herein, we disclose our results on the systematic study of radical boron migration in radical anions of type **IV** (m = 0−4) to give intermediates **V**, where the two B-atoms can interact. SET oxidation finally leads to 1,*n*-bisborylalkanes **VI** (Scheme 1B). Considering the 1,2-boron shift, the radicals **VIII** are generated from ate complexes **VII** via intermolecular hydrogen atom transfer (HAT)[4d] (Scheme 1C). Further, we will provide mechanistic insights into the reported[5] 1,2-boron migration. In all other cases, site-selective C-radical generation (see **XI**) is achieved via radical addition to B-ate complexes of type **X** (Scheme 1D).

The 1,2-boron shift to access geminal bisborylalkanes was studied first. Notably, 1,1-bisborylalkanes are important building blocks to access multifunctionalized compounds.[6,7] The current methods to prepare these compounds use *gem*-dihalides,[8] diazo compounds,[9] alkynes,[10] alkenes, etc.[11] as substrates and mostly require a transition metal to catalyze or mediate the transformation.[12] It is of interest to develop a

Scheme 1. Synthesis of 1,*n*-Bisborylalkanes via Radical Boron Migration



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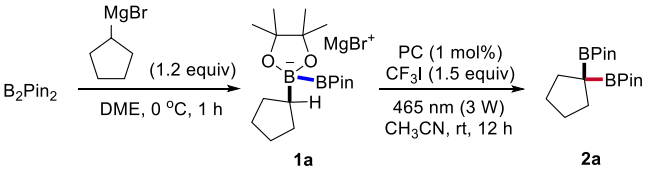
convenient method to access 1,1-bisborylalkanes from simple starting materials under transition-metal-free conditions.

In 2019, our group achieved transition-metal-free cross-coupling of organometallic reagents and organoboronic esters by intermolecular α-HAT on the corresponding boronate complexes with the trifluoromethyl radical followed by SET oxidation and ionic 1,2-alkyl/aryl migration.[4d] Encouraged by this study, we decided to apply this strategy to prepare 1,1-bisborylalkanes via diboronate complexes (see Scheme 1C). The reaction of bis(pinacolato)diboron (B_2Pin_2) with cyclopentylmagnesium bromide (1.2 equiv) targeting *gem*-bisborylalkane **2a** was selected for optimization (Table 1).

Table 1. Reaction Optimization for the 1,1-Diborylation of Cyclopentylmagnesium Bromide with B_2Pin_2[a]



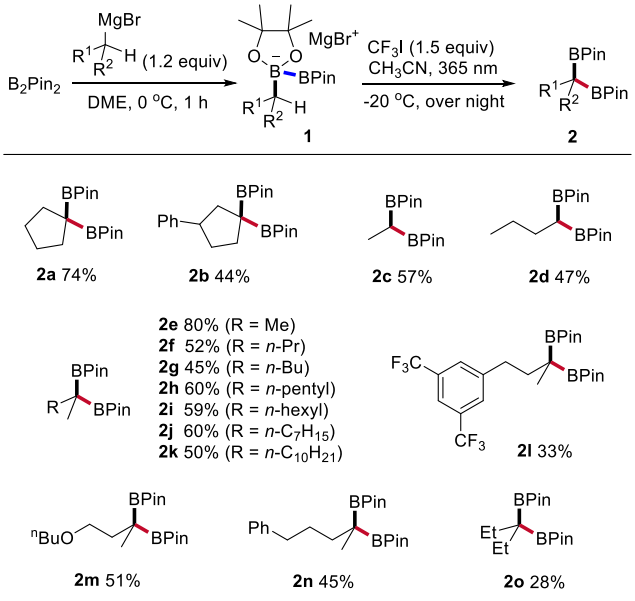
entry	PC	yield (%) 2a	yield (%) Cp-Bpin	conv (%)
1	$Ir(ppy)_3$	59	8	86
2	$Ir(ppy)_2(dtbbpy)PF_6$	62	7	85
3	$Ru(bpy)_3(PF_6)_2$	63	9	82
4	Eosin Y	56	8	83
5	Rose Bengal	35	20	82
6	Rhodamine B base	49	5	74
7[b]	$Ru(bpy)_3(PF_6)_2$	52	7	82
8[c]	$Ru(bpy)_3(PF_6)_2$	18	28	100
9	–	30	20	65
10[d]	$Ru(bpy)_3(PF_6)_2$	68	<1	82
11[e]	–	**76 (74**[f]**)**	**<1**	**91**
12[g]	–	16	17	61

[a]Reactions were conducted on a 0.2 mmol scale in CH_3CN (2 mL), conversion (conv) was determined based on the recovered bisboryl reagent, and yields were determined by GC analysis with *n*-tetradecane as internal standard on the crude reaction mixture. [b]Cyclopentylmagnesium chloride used instead of cyclopentylmagnesium bromide. [c]Bis(neopentyl glycolato)diboron ($B_2(neop)_2$) used instead of bis(pinacolato)diboron (B_2Pin_2). [d]Reaction conducted at −20 °C. [e]365 nm (3 W) at −20 °C. [f]Isolated yield. [g]Cyclopentyllithium used instead of cyclopentylmagnesium bromide.

The diboronate complex **1a** was generated in 1,2-dimethoxyethane (DME) at 0 °C. The solvent was exchanged by acetonitrile, and CF_3I was chosen as the terminal oxidant, with the CF_3-radical engaging in selective HAT abstraction at the α-position to the B-atom in B-ate complexes.[4a] Pleasingly, with tris[2-phenylpyridinato-C^2,*N*]iridium(III) ($Ir(ppy)_3$, 1 mol%) as a smart initiator[13] at room temperature, **2a** was formed in 59% yield (Table 1, entry 1). Besides **2a**, we detected 8% cyclopentylboronic acid pinacol ester (Cp-BPin) and 14% B_2Pin_2. Other metal-based and organic initiators gave similar results (entries 2−6). The complex derived from cyclopentylmagnesium chloride provided a slightly lower yield (52%, entry 7, compare with entry 3), but the yield significantly dropped to 18% with bis(neopentyl glycolato)diboron ($B_2(neop)_2$) in place of B_2Pin_2 (entry 8). Without redox initiator, the reaction also proceeded, albeit with lower efficiency (entry 9). Upon lowering the temperature, formation of cyclopentylboronic acid pinacol ester was suppressed and the yield of **2a** improved to 68% (entry 10). Initiation by simple UV (365 nm) irradiation at −20 °C led to a further improvement, providing **2a** in 76% yield (entry 11). The boronate complex derived from cyclopentyllithium gave a poor yield under the optimized conditions (16%, entry 12).

With optimized conditions in hand, we prepared a series of 1,1-bisborylalkanes from different alkyl Grignard reagents (Table 2). Both primary (**2c**−**d**) and secondary (**2a**,**b**,**e**−**o**)

Table 2. Geminal Diborylation of Alkylmagnesium Bromides—Scope[a]



[a]Conducted at 0.2 mmol scale. Isolated yields provided in all cases.

alkylmagnesium bromides engaged in the transformation to afford 1,1-bisborylalkanes in moderate to good yields (28−80%). Some functionalities such as phenyl, trifluoromethyl, and alkoxy moieties were tolerated. The reaction was found to be sensitive to sterics. For example, ate complex **1b** derived from 3-phenyl cyclopentylmagnesium bromide delivered the 1,1-bisboron compound **2b** with a decreased yield (44%) as compared to its less bulky congener **1a** (74%). Considering diboronate complexes derived from primary alkylmagnesium bromides, the less bulky ethyl derivative (**2c**) gave a slightly better yield than the corresponding butyl-ate complex (**2d**). For complexes generated from secondary alkylmagnesium bromides, the least bulky isopropyl system provided the highest yield (80%, **2e**). Due to the higher steric demand of an ethyl over a methyl group, the yield of **2o** was lower than the yields obtained for 1,1-bisborylalkanes **2e**−**n**. Of note, as Grignard reagents can be easily accessed from commercial alkyl bromides, the introduced method offers a cheap and convenient approach to 1,1-bisborylalkanes.

We noted that there is currently no general method available for the synthesis of 1,*n*-bisborylalkanes ($n > 1$),[8a,14] and we assumed the unprecedented remote radical B-migration to offer a new approach to access such compounds. Along these lines, we first addressed the 1,4-boron migration and selected **3a**, generated by reacting B_2Pin_2 with but-3-enylmagnesium bromide, as model substrate. To our delight, visible light irradiation (465 nm) of **3a** in the presence of C_4F_9I (1.5 equiv)

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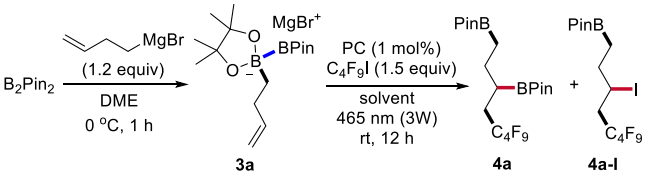
and Ir(ppy)$_3$ (1 mol%) as an initiator in CH_3CN provided the 1,3-bisborylalkane **4a** in 79% yield besides the iodine atom transfer product **4a-I** (4%) and recovered B_2Pin_2 (13%) (Table 3, entry 1). Solvent screening revealed that better yields were

Table 3. Reaction Optimization for 1,3,4-Trifunctionalization of Homoallylmagnesium Bromide—1,4-Boron Migration[a]



3a 4a 4a-I

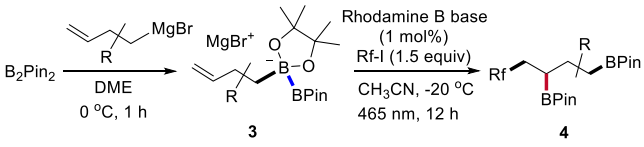
entry	PC	solvent	yield (%) 4a	4a-I	conv (%)
1	Ir(ppy)$_3$	CH_3CN	79	4	87
2	Ir(ppy)$_3$	DMSO	<1	33	85
3	Ir(ppy)$_3$	DMF	5	11	91
4	Ir(ppy)$_3$	DMA	2	2	93
5	Eosin Y	CH_3CN	76	3	77
6	Rose Bengal	CH_3CN	75	4	80
7	Rhodamine B base	CH_3CN	79	3	80
8	–	CH_3CN	44	16	94
9[b]	**Rhodamine B base**	**CH_3CN**	**87 (83[c])**	**3**	**90**
10[d]	–	CH_3CN	87	3	95
11[e]	Rhodamine B base	CH_3CN	5	–	57

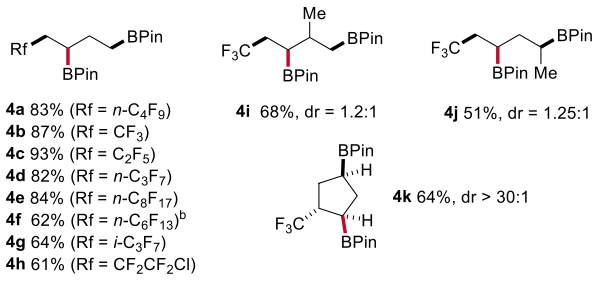
[a]Reactions were conducted on a 0.2 mmol scale in the specified solvent (2 mL), conversion (conv) was determined based on recovered bisboryl reagent, and yields were determined by crude GC analysis with *n*-tetradecane as internal standard. [b]Conducted at −20 °C. [c]Isolated yield. [d]365 nm (3 W) at −20 °C. [e]But-3-enyllithium, in situ generated by lithium/iodine exchange reaction of *t*-BuLi and 4-iodo-1-butene, used instead of but-3-enylmagnesium bromide, and THF instead of DME as solvent.

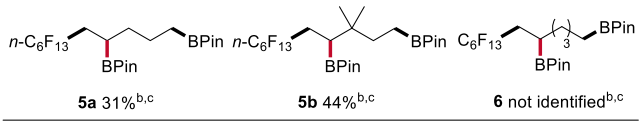
obtained in CH_3CN than in other polar solvents like DMSO, DMF, and DMA (entries 1−4). Ir(ppy)$_3$ could be replaced by organic dyes such as Eosin Y, Rose Bengal, and Rhodamine B base without diminishing the yield (76−79%, entries 5−7). Without redox initiator, the reaction also worked, but with lower efficiency (44%, entry 8), and with the cheap organic Rhodamine B base as smart initiator, the yield further increased to 87% upon lowering the temperature to −20 °C (entry 9). Notably, simple UV irradiation (365 nm) at −20 °C in the absence of any initiator provided a similar yield (entry 10). The boronate complex derived from but-3-enyllithium gave a poor yield under the optimized conditions (5%, entry 11).

A scope study of the trifunctionalization of homoallyl Grignard reagents was conducted by applying the visible light/Rhodamine B base initiation protocol (Table 3, entry 9) that proved to be more general than the UV-initiation protocol. The perfluoroalkyl radical precursor was varied first, keeping complex **3a** as the acceptor (Table 4). Linear *n*-perfluoroalkyl iodides provided the trifunctionalized 1,3-diboranes **4b−e** in excellent yields (82−93%). The less reactive *n*-perfluoroalkyl bromide also worked as C-radical precursor, but as compared to the iodides, the yield dropped slightly (62%, **4f**). With perfluoroisopropyl iodide, a 64% yield of **4g** was obtained. 1-Chloro-2-iodotetrafluoroethane reacted chemoselectively at the I-bearing C-atom to give **4h** (61%). Iodoacetonitrile and

Table 4. 1,4- and 1,5-Boron Migration Reactions[a]







[a]Conducted on a 0.2 mmol scale. [b]*n*-$C_6F_{13}Br$ was used. [c]Reaction conducted at room temperature.

ethyl iodoacetate gave only trace amounts of the targeted products (not shown). Unfortunately, diastereoselectivity for the 1,4-boron shift in open-chain systems was very low (see **4i,j**). However, for the cyclic rigid diboronate complex **3k**, 1,4-*syn*-boron-migration selectivity was complete, and also the initial CF_3-radical addition occurred with excellent stereocontrol (*trans*-addition) to provide product **4k** as a single diastereoisomer (64%).

With 4-pentenylmagnesium bromide as starting material, we next addressed the 1,5-boron migration and noted that, with perfluoroalkyl iodides as C-radical precursors, the I-atom transfer compounds **5-I** (not shown) were formed as major products and targets **5** were obtained in low yields. Therefore, we had to switch to the less reactive bromides. A moderate 31% yield of **5a** was achieved with *n*-perfluorohexyl bromide under the conditions optimized for the 1,4-boron shift. The yield could be slightly improved to 44% (see **5b**) by installing a 3,3-dimethyl substitution pattern, benefiting from the Thorpe−Ingold effect.[15]

We also attempted the 1,6-boron migration on the homologous diboronate complex derived from 5-hexenylmagnesium bromide with CF_3I as the radical precursor. However, the targeted 1,5 bisborylalkane was not identified, and the reaction provided the corresponding I-atom transfer product as the major product. Switching to *n*-perfluorohexyl bromide, the 1,6-boron migration product **6** could not be identified, indicating that this migration cannot compete with other processes.

Finally, to complete the series, we tackled the 1,3-boron migration. The required diboronate complex was formed by the reaction of allylmagnesium bromide with B_2Pin_2. However, neither with perfluorobutyl iodide nor with its bromide was any 1,2-bisborylalkane identified, and B_2Pin_2 was formed in a large amount (85%) as major product. Hence, SET oxidation of allyl-B_2Pin_2MgX under all tested conditions generating the stabilized allyl radical was too fast, and therefore this alkene could not act as a radical acceptor under the applied conditions. Since we did not find any suitable system to

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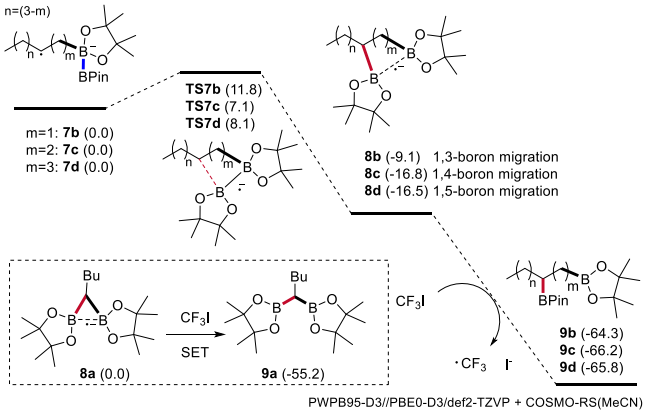
experimentally investigate the 1,3-boron migration, we decided to approach that problem by using computational chemistry. DFT calculations[16] were performed on a series of pent-(*m*+1)-yl-substituted radical anions **7a–d** (*m* = 0–3, Scheme 2) to get a full picture on the boron migration aptitude in these diboronate radical anions.

Scheme 2. DFT Model Calculations of Diboronate Radical Anion Rearrangements



In the study of the reactions, we have found bisborane radical anion intermediates **8** with the spin localized in a B–B single electron bond, similar to those found in the 1,2-carboboration of alkenes with B_2Cat_2.[17] In the case of the 1,2-boron migration (*m* = 0),[18] the initial radical **7a** exhibits this structure already, which means that 1,2-boron radical migration is a spontaneous and barrierless process. In the case of the distonic (*m* > 0) radical anions **7b–d**, a cyclization occurs with low free energy barriers (7–12 kcal/mol) to form the analogous intermediates **8b–d** exergonically. These will readily transfer—likely assisted by the MgBr counter-cation[17c]—one electron to the iodo reagent and regenerate the trifluoromethyl radical, forming the 1,(*m*+1)-bisboryl-alkanes **9a–d**. Compared to the 1,4-boron migration, the barrier for the radical 1,3-boron migration increases (from 7.1 to 11.8 kcal/mol). The 1,5-boron migration (8.1 kcal/mol) showed a slightly higher barrier than the 1,4-shift. In the case of radical anion **7b** (1,3-boron migration), in the computation we did not find any indication for facile *β*-fragmentation leading to the B_2Pin_2-radical anion along with 1-pentene. This supports our suggestion that the observed formation of B_2Pin_2 in the reaction with allyl-B_2Pin_2MgX is likely caused by initial SET oxidation of allyl-B_2Pin_2MgX rather than *β*-fragmentation of the corresponding distonic radical anion of type **7b**.

In summary, radical 1,2- and 1,4-boron migration reactions in diboronate complexes derived from B_2Pin_2 are useful preparative processes to access synthetically valuable 1,1- and 1,3-bisborylalkanes. Considering the 1,3-functionalized compounds, high selectivity in the boron migration can be achieved in cyclic systems. The 1,5-boron migration leading to 1,4-bisborylalkanes also occurs, albeit with lower efficiency. The experimental findings on the B-shift were supported by DFT calculations, which further revealed the currently experimentally inaccessible 1,3-boron migration to be feasible. Since B_2Pin_2 is commercially available and the Grignard reagents are readily prepared from the corresponding alkyl bromides, the introduced methods offer a straightforward approach to 1,*n*-bisborylalkanes.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.0c03058.

Experimental details and characterization data, DFT calculations, and NMR spectra of new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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